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# Cardiac injury, ARDS and COVID-19 meta-analysis validity - Correspondence in response to Santoso et al

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Title: Cardiac injury and ARDS meta-analysis validity – correspondence in response to Santoso et al

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Dear Editor,

In the course of writing a rapid review for the University of Oxford, we came across an interesting and timely systematic review and meta-analysis in the *American Journal of Emergency Medicine* by and colleagues (1). This paper was of note to us because it included a meta-analysis on acute respiratory distress syndrome (ARDS) and cardiac injury, based on two papers - one by Shi (2) and another by Wu (3). On reading the paper by Wu, we have significant concerns about the inclusion of this study in Santoso's meta-analysis as we believe it currently underpins an inaccurate conclusion that cardiac injury is not significantly associated with increased risk of ARDS in COVID-19 by Santoso.

In Figure 3 in Santoso, they describe Wu as 26 cases of ARDS (11 cases of ARDS with cardiac injury, and 15 cases of ARDS with no cardiac injury). When we examined the Wu paper, we found a composite outcome of respiratory failure, ARDS and sepsis was reported, totalling 26 cases across the different troponin levels (Table 2 in Wu). Further, when we studied Table 1 in Wu, 26 patients are described as having respiratory failure/ARDS/sepsis. This is broken down as 20 with respiratory failure and 6 with ARDS or sepsis. Even if one assumes that all of those cases were ARDS, that gives a total of 6 ARDS cases in this paper, contrasting with the 26 used for Santoso's meta-analysis.

There are conceivable alternative explanations for these figures, for instance perhaps all of the respiratory failures were caused by ARDS and Wu used a counterintuitive way of presenting the data by separating these out from the 6 ARDS or sepsis cases. However, from what we currently have access to, it seems most likely that Santoso's meta-analysis for ARDS has been based on composite endpoint data. This is concerning, particularly when there is evidence ARDS was a minority diagnosis. Moreover, the conclusion of Santoso runs counter to Shi's JAMA Cardiology paper, which was the other paper included in Santoso's meta-analysis, which did report on purely ARDS cases and cardiac injury and did find a statistically significant association.

Screening and data extraction in Santoso were performed by two authors, which is good practice and reduces the probability of a simple error. We are therefore curious to learn whether the authors had contact with Wu et al and have insights into the Wu data that are not immediately apparent to readers. If so, we would appreciate Santoso et al sharing this information publicly as it would inform our research and no doubt that of others.

We look forward to having our confusion addressed by the authors and thank them for their work.

References

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